

CLAIMS*Suba*

1. The use of:
 - (i) EtxB, CtxB or VtxB free from whole toxin;
 - (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
 - (iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding;
- 5 as an immunomodulator for a vaccine against infectious diseases.
- 10 2. ^{A method} ~~The use~~ according to claim 1, wherein the immunomodulator is EtxB free from whole toxin.
- 15 3. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein the infectious disease is one for which the infectious agent is a member of the herpes virus family.
- 20 4. ^{A method} ~~The use~~ according to claim 3, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of HSV-1, HSV-2, EBV, VZV, CMV, HHV-6, HHV-7 and HHV-8.
- 25 5. ^{A method} ~~The use~~ according to claim 4, wherein the infectious agent is selected from the group consisting of HSV-1, HSV-2, CMV or EBV.
- 30 6. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein the infectious disease is caused by an infectious agent, and the infectious agent is an influenza virus.
- 35 7. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein the infectious disease is caused by an infectious agent, and the infectious agent is a parainfluenza virus.
8. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein the infectious disease is caused by an infectious agent, and the infectious agent is a respiratory syncytial virus.
9. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein

the infectious disease is caused by an infectious agent, and the infectious agent is a hepatitis virus.

10. ^{A method} ~~The use~~ according to claim 9, wherein the infectious agent is selected from the group consisting of hepatitis A, B, C and D viruses.

11. ¹ ~~The use~~ according to claim 10, wherein the infectious agent is a hepatitis A virus or a hepatitis C virus.

12. ¹ The use according to claim 1 ~~or 2~~, wherein the infectious disease is meningitis.

13. ^{A method} ~~The use~~ according to claim 12, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Neisseria meningitidis*, *Haemophilus influenzae* type B and *Streptococcus pneumoniae*.

14. ^{A method} ~~The use~~ according to claim 1 ~~or 2~~, wherein the infectious disease is pneumonia or a respiratory tract infection.

15. ^{A method} ~~The use~~ according to claim 14, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Streptococcus pneumoniae*, *Legionella pneumophila* and *Mycobacterium tuberculosis*.

16. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is a sexually-transmitted disease. ^{A method}

17. The use according to claim 16, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Neisseria gonorrhoeae*, HIV-1, HIV-2 and *Chlamydia trachomatis*.

18. ^{method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is a gastrointestinal disease.

19. ^{A method} The use according to claim 18, wherein the infectious disease is caused by an infectious agent,

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and the infectious agent is selected from the group consisting of enteropathogenic, enterotoxigenic, enteroinvasive, enterohaemorrhagic and enteroaggregative *E.coli*, rotavirus, *Salmonella enteritidis*, *Salmonella typhi*, *Helicobacter pylori*, *Bacillus cereus*, *Campylobacter jejuni* and *Vibrio cholerae*.

20. ^{A method} The use according to claim 1 ~~or 2~~, wherein the infectious disease is a superficial infection.

21. ^{A method} The use according to claim 20, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Staphylococcus aureus*, *Streptococcus pyogenes* and *Streptococcus mutans*.

22. ^{A method} The use according to claim 1 ~~or 2~~, wherein the infectious disease is a parasitic disease.

23. ^{A method} The use according to claim 22, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of malaria, *Trypanasoma* spp., *Toxoplasma gondii*, *Leishmania donovani* and *Oncocerca* spp.

24. A vaccine composition for use against an infectious disease, which infectious disease is caused by an infectious agent, wherein the vaccine composition comprises an antigenic determinant and an immunomodulator selected from:

- (i) EtxB, CtxB or VtxB free from whole toxin;
- (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
- (iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding;

wherein said antigenic determinant is an antigenic

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determinant of said infectious agent.

25. A vaccine composition according to claim 24 in which the infectious disease is HSV-1 infection and wherein the antigenic determinant is an antigenic determinant of HSV-1.

26. A vaccine composition according to claim 24 or 25 in which the immunomodulator is EtxB free from whole toxin.

27. A vaccine composition according to claim 24, 25 or 26 in which the immunomodulator and the antigenic determinant are separate moieties.

28. A vaccine composition according to claim 24, 25 or 26 in which the immunomodulator and the antigenic determinant are linked by a bifunctional crosslinking reagent,

29. A kit for vaccination of a mammalian subject against an infectious disease, which kit comprises:

a) one of the following agents:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or

(iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding; and

b) an antigenic determinant which is an antigenic determinant of the infectious disease, for coadministration with the said vaccine immunomodulator.


30. A method of preventing or treating a disease in a host, which method comprises the step of inoculating said host with a vaccine comprising at least one antigenic determinant and an immunomodulator, where the immunomodulator is:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having

Gb3-binding activity; or

(iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding.

5  §1. The use of:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or

10 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding
or Gb3 binding

to upregulate the production of antibodies at mucosal surfaces.

15 32. The use of:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtXB, having GM1-binding activity, or an agent other than VtXB having Gb3-binding activity; or

20 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding
or Gb3 binding;

as an immunomodulator in a vaccine, to prolong antigen presentation and give sustained immunological memory in a mammalian subject.

33. A vaccine composition for use against an infectious disease, which infectious disease is caused by an infectious agent, which vaccine comprises an antigenic determinant and a immunomodulator selected from: ^{the group consisting of}

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; ^{and} ~~or~~

35 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding

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or Gb3 binding;

wherein said antigenic determinant is an antigenic determinant of said infectious agent and wherein the immunomodulator prolongs presentation of the antigenic determinant and gives sustained immunological memory.

34. \ The use of:

- (i) EtxB, CtxB or VtxB free from whole toxin;
- (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
- (iii) an agent which has an effect on vesicular internalisation mediated by GM1-binding or Gb3 binding;

in a conjugate with antigen or antigenic determinant to target the delivery of said antigen or antigenic determinant to the cytosol or nucleus of an antigen presenting cell.

35. The use of:

- (i) EtxB, CtxB or VtxB free from whole toxin;
- (ii) an agent other than EtxB or CtxB, having GM1-binding activity; or an agent other than VtxB having Gb3-binding activity; or
- (iii) an agent which has an effect on vesicular internalisation mediated by GM1-binding or Gb3 binding;

in a conjugate with antigen or antigenic determinant to upregulate the presentation of said antigenic determinant, or an antigenic determinant derived from said antigen, by MHC class I molecules.

36. A vaccine composition which comprises:

- a) EtxB, CtxB, or an agent other than EtxB or CtxB which has GM1-binding activity; and
- b) an EBV antigen

for use in the treatment and/or prevention of EBV-associated diseases.

37. A therapeutic composition which comprises:

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